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Differences existing between USA and Europe in opioids purchase on Internet: An interpretative review

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Title: Differences existing between USA and Europe in opioids purchase on Internet: an interpretative review

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Abstract

Background:

Opioids e-commerce represents an important public health issue. While the literature describes this phenomenon in the USA, the studies about this topic are scarce in Europe. This review aims to describe the state of the art of the online opioids commerce and to explore the factors influencing the opioids e-commerce.

Methods:

Scientific literature available via four bibliographic databases (PubMed, Cochrane Collaboration, ISI Web of knowledge and Scopus) was screened on June 2012. Keywords used were “Internet and opioids”, “Online and opioids”, “Web and opioids”, “Opioid selling”, “Opioid business”, “Opioid buy”, and “Opioid sale”. After the selection, 31 articles were finally identified as meeting the inclusion criteria.

Results:

The online market of opioids had experienced a boom thanks to the discount prices, the poor monitoring actions, the quickness and easiness of acquiring of these drugs. Legislation on the sale of drugs online differs among the countries. We found that the opioids e-commerce and its consequences are detailed for the USA context, while there is a lack of knowledge in Europe.

Conclusions:

Public health impact of online purchase is worthy of consideration and additional research, considering the potential underestimation of the phenomenon. Public health interventions can be indeed hampered by the lack of knowledge of professionals about this topic.

Keywords

Internet, opioids, purchase

Main text

Introduction

Drug addiction is still a great concern in the industrialized countries, regardless of age class (Compton & Volkow, 2006a, 2006b). As previously reported by Compton et al., the abuse of prescription and over the counter medications, such as painkillers, is comparable to misuse recorded for the illicit drugs, especially among the adolescents. The most frequent drugs taken for recreational purposes in the USA are the opioid analgesics, followed by marijuana (Compton & Volkow, 2006a, 2006b; Johnston et al., 2004). In the USA, the annual incidence of opioid analgesics abuse reached the impressive figure of 2.4 million of addicted people in 2001. In the last decade the incidence has increased and, in 2010, about 12 million Americans reported non-medical use of prescription painkillers (Substance Abuse and Mental Health Services Administration, 2003). The Center for Disease Control and Prevention considered the analgesic opioids abuse and overdoses as a growing public health epidemic. To date, indeed, there are more overdose deaths related to opioid analgesics consumption (such as Vicodin, Oxycontin and Oxycodone) than heroin and cocaine combined, and the nonmedical consumption of these drugs costs around \$72.5 billion to the health insurances annually. Nearly half a million of the emergency department visits in 2009 were due to people misusing or abusing painkillers (Center for Disease Control and Prevention, 2011; Substance Abuse and Mental Health Services Administration, 2003). In the 2000s, different reports have cited a remarkable increase of opioid use worldwide, particularly among young people (Johnston et al., 2004; Substance Abuse and Mental Health Services Administration, 2003, 2004). As reported by Forman et al., the most important institutions responsible for the illicit drug control reported that the Websites selling drugs without control may play a specific role in the diffusion of this harmful market (Forman et al., 2006b; Office of National Drug Control Policy, 2004; Volkow). The increasing sale is due to a higher number of legal prescription and to the growth of the illegal market. In particular, the Internet has opened a new and easy way of access to this kind of drugs. Anyone with a credit card, indeed, can buy any kind of opioids without a medical supervision (Compton & Volkow, 2006b). In this regard, the World Wide Web, indeed, counted around 2.27 billions of users worldwide at the end of 2011 (Internet World Stats, 2012). The Pew Internet & American Life 2005 Project reported that 66% of US Internet users made purchases online, and the same percentage of responders reported to look for health and medical information on the Web (Rice, 2006). This growing phenomenon, called e-health, was then confirmed

Also in the European area by other researches (Bert et al., 2013; Giacometti et al., 2013; Kummervold et al., 2008; Siliquini et al., 2011, 2012). In Europe, the issue of the drugs online purchase seems to be less known and investigated. The data available, indeed, are poor and this phenomenon could be underestimated. Only one survey, called the Psychonaut 2002 Project (Schifano et al., 2006), funded by the European Union (EU) with the aim of investigating the online drug community, was conducted in Europe in order to fill the gaps in the existent knowledge about this topic. This survey describes the ways of access of several drugs categories, taking into account, the psychiatric medications, plants and herbs, anabolic steroids, hallucinogens and opioid analgesics. In Europe, however, there are no reviews about this specific topic and poor involvement and alert are shown by the media and the public opinion. Our review aims to describe the state of the art of the online opioids commerce and to identify and explore the factors that influence the sale and the purchase of opioids without medical prescription through the Web providers, by making comparison between the USA and Europe.

Materials and methods

Scientific literature and legislations considered in this review include national and international journal articles, both academic and non-academic, available and accessible via four commonly used bibliographic databases: PubMed, Cochrane Collaboration, ISI Web of knowledge and Scopus. A detailed bibliographic search was conducted, with keywords used alone or combined using the builder OR and/or AND. The keywords used were “Internet and opioids”, “Online and opioids”, “Web and opioids”, “Opioid selling”, “Opioid business”, “Opioid buy”, and “Opioid sale”. The aim was to access a broad range of literature around the sale of opioids online. All searches were carried out on June 2012 and were not limited by date. The trained members of the project team reviewed the bibliographic details for each item independently. Articles were selected according to the following criteria:

- Availability of free full text of the paper online, i.e. open access or available via the host institution’s e-library of online journals.

- Language of the paper: English.

- Inclusion of the paper of explicit references of opioid drugs available on the Web.

- Agreement of the reviewers about the opportunity of paper inclusion (disagreements have been overcome through a face-to-face meeting).

Relevant literature reviews were included but used only for cross-validation of the findings of this review. The articles matching the criteria were included and subjected to further analysis. Figure 1 shows the flow diagram of the bibliographic search. Initial search using the above mentioned keywords returned 694 items with PubMed, 4 items with Cochrane Collaboration, 217 with ISI Web of knowledge and 304 with Scopus, for a total of 1219 articles. After the removal of duplicates, 121 items were reviewed by all the members of the project team. The reviewers agreed, after the revision of titles and abstracts, 46 articles deserved a closer examination, as strictly related to the topic of interest. Among these, 31 were identified as meeting the inclusion criteria and specifically focused on opioids e-commerce (Table 1).

Results

USA

Legislation governing the sale of drugs online United States The drugs e-commerce regulation in the USA is very clear. The purchase of any drug must be done through a properly accredited Internet site (Verified Internet Pharmacy Practice Site – VIPPS), which requires a valid prescription for the sale. However, the literature reports many experiences witnessing a relative easiness in legal and illicit drugs purchase through the Web (National Association of Boards of Pharmacy).

In the USA, the illicit substances and legal drugs which may be subjected to abuse are divided into five categories named schedules (listed in the Controlled Substances Act, see Table 2) (Controlled Substances Act, 1970; Forman et al., 2006a). Despite this legislation and the Controlled Substances Act, the number of Websites selling opioids illegally is very high. Online stores, indeed, can be hosted and registered anywhere in the world. The advertisement, the sale and the delivery of products can be carried out with relative anonymity and convenience – with little regard for the laws of other countries. Many countries have introduced, indeed, drug policies that differ from those of the USA or have similar laws but less control and enforcement. Some interventions, aiming to solve this issue, started since 2002 in order to uncover and close non-authorized online pharmacies. As example, the operation done by the U.S. Drug Enforcement Administration (U.S. DEA) called “CYBERx” discovered 22 no-prescription online pharmacies, while another investigation done in 2004 by the U.S. Government Accounting Office (U.S. GAO) reported 9 of 11 online pharmacies delivered opioid analgesics without a prescription (Boyer & Wines, 2008; Drug Enforcement Administration, 2005; General Accounting Office, 2004a, 2004b).

Europe

In Europe, the online commerce of drugs is uneven, differing considerably according to the country of reference. In some countries, it is possible to buy any type of product online by submitting regular prescription, while in other countries, instead, the drugs e-commerce is contrary to current regulations and therefore illegal. For instance, in Italy, the only products that people can legally buy online are food supplements and beauty products that do not require a specific prescription. However, in 2011 a new European legislation was introduced to force all countries to adapt their rules to the EU directives within 18 months (Official Journal of the European Union, 2011). This legislation provides a much more rigid control of the e-commerce. The online pharmacies must obtain a special permission and all Websites involved in the drugs e-commerce will have to acquire one common logo recognized throughout the EU. The consumers will be able to recognize whether the Websites are registered as licensed pharmacy or not. Furthermore, a central control Website monitoring online pharmacies and the drugs commerce will be created both at national and European level. Finally, a system based on security codes to ensure the authenticity and identification of individual packages of drugs bought online will be realized. The European Commission, in cooperation with the European Medicines Agency (EMA) and the Member States, will undertake actions to promote awareness campaigns in order to warn about the risks related to medicinal products purchase from illegal sources via the Internet.

Online market of opioids

The authors aimed to analyze and report the existing literature about the easiness of finding drugs. In order to achieve this aim, the top five search engines in western countries (Google, Yahoo!, Ask.com, Bing.com and MSN) were selected and consulted. The literature shows as No-Prescription Websites (NPWs) and are very easy to find through the most common and used search engines, such as Google and Yahoo (Forman, 2003; Forman & Block, 2006).

USA

In more than 50 Internet-monitoring surveys, in which search terms related to specific opioids or similar drugs (such as “codeine” and “Vicodin”) were used, more than 50% of the results led to Websites that offered to purchase opioid medications without a prescription (Forman et al., 2006a). Using “no prescription” as keyword, it is possible to find a greater number of Websites (with an increase of 60–80% of results retrieved). Commonly, the Websites and the pharmacies selling opioids online are, according to all the Internet-based survey, pervasive and very often easier to find and access than the Websites only providing information. The access to opioids commerce is frequently not restricted to people having medical prescription; sometimes the consumers can gain access to drugs only after filling an online questionnaire or interview/consultation (Drug Enforcement Administration, 2001; General Accounting Office, 2004b).

A study carried out by the National Center on Addiction and Substance Abuse at the Columbia University analyzed 495 Websites selling drugs online. Around a third (157) of these Websites were selling controlled prescription drugs, while 90% did not require any prescription or offered only an “online consultation”. The opioids most frequently sealed were Codein, Dyphenoxilate, Hydrocodone, Hydromorphone, Meperidine, Oxycodone and Propoxyphene (The National Center on Addiction and Substance Abuse at Columbia University, 2004). Another interesting study analyzed how much the opioids were mentioned in online chat. Butler et al. (2007) found that the three most mentioned opioids were OxyCotin, Vicodin and Kadian, with more than 48 000 posts related to this topic, unfortunately without any information about the purchase. The U.S. GAO also conducted an investigation contacting some online pharmacies to highlight the easiness of online of opioids. This investigation reported that from the non-authorized pharmacies, people can buy, e.g. hydrocodone, without providing a prescription (General Accounting Office, 2004b). The easiness of

purchase is confirmed by another analysis done by the National Center on Addiction and Substance Abuse at Columbia University. They demonstrated that it could be easy for children to buy online some potentially lethal drugs. In their analysis, they also underline how only the 10% of the Websites analyzed required a prescription (Drug Enforcement Administration, 2001). Although all authors agree that opioids abuse and the number of Websites offering the purchase are increasing day by day, not everyone agree that the real abuse is related to e-commerce (Giacometti et al., 2013). In particular, a study carried out by the Washington University suggests that the role of the Web has a new dangerous way to buy opioids appears to be based on no empirical evidence.

Europe

Specific literature and data about online opioids commerce in Europe is still lacking. A 2008 French survey, conducted in 142 addictive care centers and enrolling 5542 subjects, described the consumption of several substances including 63.8% of prescription drugs, including opioids. Among them, 11% were illegally obtained. The different illegal acquisition ways reported were “street market” (77.6%), “gift” (16.6%), “theft” (2.3%), “forged prescription” (2.3%), and “Internet” (0.7%) (Frauger et al., 2012). These results confirm other available data which report that the role of Internet in the drugs commerce may be overstated (Giacometti et al., 2013; Inciardi et al., 2009; McCabe et al., 2007). The Psychonaut Project analyzed, instead, 150 Websites and about 800 Webpages retrieved searching the keyword “Tramadol” on the leading search engine Google. They found a high number of commercial Websites and only few private and institutional/governmental Websites. This survey reported also an interdiction of “online” prescriptions in Germany, while in Netherlands two2 Websites offer online prescription. Many Websites surveyed assume a pro-drug consumption attitude and invite to use tramadol as a regular analgesic drug (“...if the doctor prescribes this drug it can’t be harmful”) and give advice on how to get own doctor to prescribe an opioid analgesic (Bert et al., 2013; Siemann et al., 2009).

The negative effects of opioids sale on the Web

Several adverse events of opioids e-commerce, which caused hospitalization or in some cases the death, were reported. This phenomenon is true and ubiquitary for the majority of the available opioids, and the consequent effects are probably underestimated and not adequately reported by the media and the scientific community. The following paragraphs include some cases, reported by literature, describing the negative effects of illegal substances on subjects that bought them on the Web.

United States

Lieberman reported the case of a 26 years old patient in the USA, already followed by the mental health services for social phobia, that was able to legally obtain a huge quantity of opium poppies online. These poppies, used to produce infusions, caused in the young man a dependence with a consequent need of hospital admission and rehabilitation (Lieberman, 2001). Bailey et al. (2010) describe another dramatic case, related to the poppy seed tea consumption, with a fatal conclusion. The patient, a 42 years old U.S. man, died after the contemporary consumption and intoxication of several drugs, such as phenazepam, morphine, codeine and thebaine. The police investigation discovered that the man was used to buy these kind of substances online and that the poppy seed tea, taken prior to his death, could be related to the exitus. Logan et al. (2009) reported five cases of American adolescents who died after an acute intoxication due to Dextromethorphan abuse. This drug was bought on Internet for recreational purposes in many occasions by the same supplier. The police identified the supplier responsible thanks to a sixth adolescent that survived. Recently, the analgesic opioids use has caught media attention for a tragic crime story. In Denver, Colorado,

indeed, a young man was arrested for the killing of 14 people at the film premiere of the movie “Batman – The Dark Knight Rises”, also known as the “Batman Massacre”. After the massacre, the murderer James Holmes confessed to detectives that he had taken the drug Vicodin (Allen, 2012). Among the side-effects of Vicodin euphoria, paranoia and, in some cases, hallucinations, altered mental states and “unusual thoughts or behavior” can be mentioned (Drugs.com – Drugs Information Online). However, even if it is impossible to confirm a relationship between the Vicodin use and the “killing behavior”, this fact suggests to reflect upon the potential dangers of the free circulation of these drugs and their easiness of online purchase.

Europe

In Europe, we found the study by Kronstrand et al. describing, instead, nine cases of fatal overdoses, occurring in Sweden in a short period of time. The illegal drug involved was the Internet-available “Krypton”, composed by powdered Kratom leaves (medicinal plant in Southeast Asia) with the addition of another mu-receptor agonist, O-desmethylnaloxone. Internet Websites claim that Krypton is not dangerous for health and quite safe (Kronstrand et al., 2011). To our knowledge, following these case series, the only action taken by the authority against the Web suppliers was the closure of the Websites incriminated.

The point of view of the consumer: benefits and disadvantages of the online purchase

Both in American and European perspective, the e-commerce of opioids can bring some apparent “benefits” for the consumer but at the same time several relevant disadvantages have to be taken into account. The reasons related to Web- buying in online pharmacies and Websites are pretty clear. First of all, the price of drugs and products bought online is usually lower than the same drugs on sale in physical pharmacies. This difference of price can be really important, reaching discounts until the 80% of the original price (International Drug Mart, 2008; Klein, 2011). Moreover, the lower price, often due to the importation of drugs from foreign countries, can improve the access to therapies, especially in those countries with a national health service based on private insurances, such as USA (Ornes, 2006). Another convenience is the quickness and efficiency of the online purchase. Drugs and products are easily ordered with a simple process completed in a very short time, much more rapidly than the usual way of purchase. Finally, the range of drugs and opioids available online is unlimited and accessible at all times (Klein, 2011; Raine et al., 2009). The e-commerce could be profitable and favorable for the consumers, but it is essential to highlight the huge disadvantages related to this practice (Weiss, 2006). First, the lack of monitoring and the self-medication may result in an increased risk of drugs abuse, even more in the case of opioids due to their specific addictive features (Nielsen, 2009). The monitoring deficiency is also related to the lack of a proper evaluation performed by a doctor or a psychiatrist. It is possible that the Web-based questionnaires used instead of medical prescription in many of these Websites and online pharmacies can lead to misdiagnosis and often an overestimation of the patient’s real needs. Proper diagnosis and treatment could be delayed with life-threatening consequences and the absence of monitoring for side effects by a real physician may create additional risks for the opioid users. Furthermore, the risk of counterfeit and falsification of drugs and products bought on the Web is very high. The dangers related to this issue are remarkable. The drugs sold at so discount prices, indeed, can be linked to an incorrect active principle, to a production under basic sanitary standards, or to a drugs that have already passed their expiration date (Lu, 2003). Finally, the intrinsic characteristics of online commerce expose the consumer to some risks equally worthy of attention, such as the privacy violation and the poor security of money transitions through credit cards.

Discussion

To our knowledge, this is the first review of scientific literature describing the state of the art of the online opioids commerce and its consequences with a focus on the comparison of the scenario in the USA and Europe. The phenomenon of Internet purchase of opioids is rising, as witnessed by the data reported from the International Narcotic Control Board showing that analgesics drugs (including opioids) are the most sold on the Web, among narcotics (United Nations, 2007). This issue is particularly perceived in the USA, just considering that in the period 2002–2005 an increase of 29% in the Oxycodon use among adolescents was registered (The Internet and Adolescent Non-medical Use of Prescription Drugs). This rise in the licit and illicit online sale of drugs can be confirmed also by performing researches using a search engine. As examples, with the keyword “buy Viagra”, on Google 29 200 000 of results were retrieved in May 2011, while 1 year later the results were 482 000 000. To date, NPWs are still poorly known and further research is needed to describe all the implications of these Internet retails on consumers health. The boom experienced by NPWs can be easily attributed to the high profits related to this illegal market. The business is evolving and the number of industries who aim to join the legal market (pharmacies, parapharmacies, herbalist’s shops) is growing. As previously suggested, the main issue is that the availability of information about the risk of abuse, addiction and dependence are generally lacking on these Websites. The availability of drugs without prescription removes health care professionals from the prescription process, introducing additional risk for drug misuse, abuse, dependence and overdose. This circumstance seems even more alerting considering that Websites and online pharmacies not requiring a medical prescription are potentially dangerous, especially for teenagers. This age class, indeed, who represents the one in which drug use typically begins, is also the one who most frequently uses the Web (Gerstein & Green, 1993; Lenhart et al., 2005; National Institute on Drug Abuse, 2003). The NPWs usually appear like professional or institutional Websites with attractive images and misleading messages (Gaul & Flaherty, 2003). A previous analysis, conducted by Forman and Lauren, reveals how these Websites often include images of doctors and nurses and logos of international pharmaceutical companies in order to seem legitimate in the sale. A disclosure statement of their legal status is often included in their homepage but in many cases is not real and the Website is not officially registered and approved by country-specific legal regulations (Forman & Block, 2006; Gaul, 2003). Public health professionals working in prevention and health promotion have to enhance their efforts towards the diffusion of prevention messages on the Web, especially for those substances, such as opioids, that are most frequently abused (Katz et al., 2008). The creation of an official list of approved and legitimate Web retailers and drugs suppliers is then urgently needed at international level. Monitoring the market through a severe regulation can lead to an improvement in the safety of consumers. In this regard, in the USA there are already authorities specifically created for the control of this online business. Among these, a prominent role is played by the U.S. DEA and by the U.S. GAO. As example, with an operation called “CYBERx” the DEA closed 22 NPWs that sold opioid analgesics but unfortunately, despite the apparent success of this action, follow-up studies reported that NPWs offering opioids remained widely available to consumers (Drug Enforcement Administration, 2005). This is easily explainable since very often the drugs buyers rely on servers that are not registered in the country of residence and, therefore, not subjected to the local legislation and hardly traceable. In Europe, instead, the monitoring of illegal online opioids market is in many cases done by law enforcement agencies and only in recent times the EU promoted a specific action to focus the attention on the need of reduce and control illicit businesses in this field. This review has some limits that need to be discussed. First of all, we can assume that the available data on online opioids purchase are underestimated because only the cases with more severe consequences that focused the media attention are usually reported. Use and abuse of this kind of drugs are often less declared by consumers and therefore data can suffer from poor reporting and can be no completely reliable. Moreover, our inclusion criteria did not allow a comprehensive review of the available data existing in scientific literature, for example the limit of language (“English”) restricted our investigation field. The business of legal and illicit online purchase of opioids

is increasing worldwide and can lead in some cases to dramatic consequences. However, this phenomenon should be contextualized in the global reality of opioids use and abuse, that have large diffusion in the society through different ways of sale. Previous studies suggested poor percentages of Web use in the opioids purchase (1–6%) and a greater confidence of people in local pharmacies than in Internet-based pharmacies (Frauger et al., 2012; Giacometti et al., 2013). The current scenario demonstrates that the application of the new ways of communication could have positive effects on health (de Waure et al., 2012), but it is important to monitor and control the use of these instruments, such as the Internet, in order to avoid some negative effects.

In conclusion, the public health impact on Web consumers is worthy of consideration and additional research, considering the potential underestimation of the cases. Indeed, the success of public health interventions and prevention actions can be hampered by the lack of knowledge in this field and by the underestimation of cases due to poor attention of public opinion and professionals about this topic.

Figure 1 - Decision points in the review process: the flow chart.

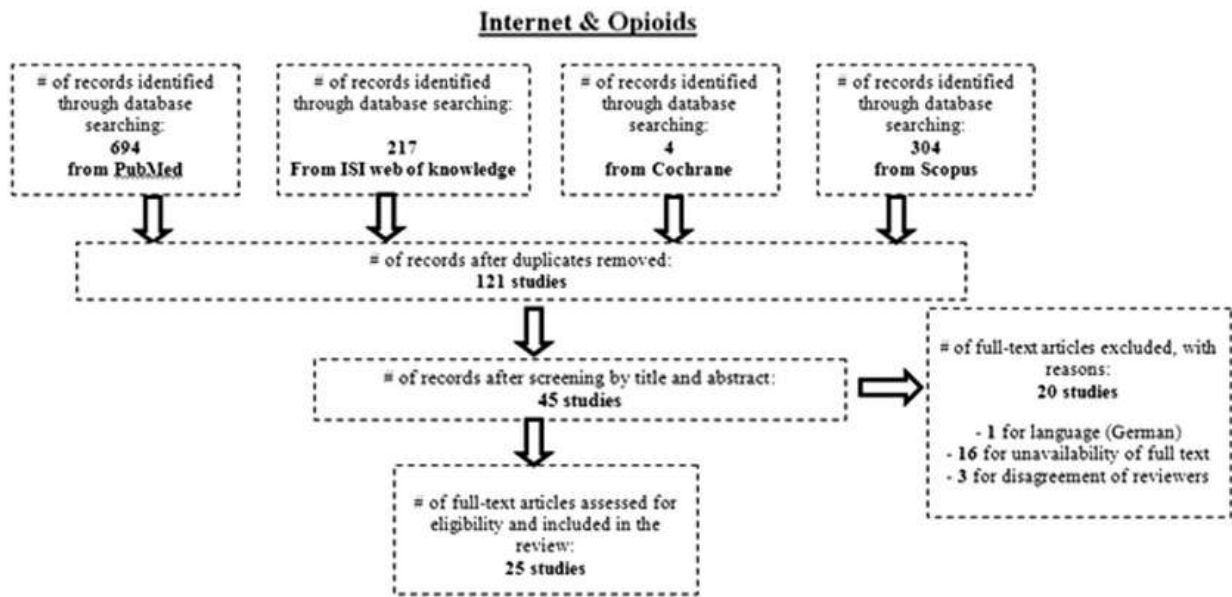


Figure 1. Decision points in the review process: the flow chart.

Table 1. Papers included in the review.

Author	Year	Title	State	Objective
Boyer EW et al.	2008	Impact of Internet Pharmacy Regulation on Opioid Analgesic Availability	USA	Survey on the availability of prescription opioid analgesics from online pharmacies
Butler SF et al.	2007	Internet Surveillance: Content Analysis and Monitoring of Product-specific Internet Prescription Opioid Abuse-related Postings	USA	Systematic analysis of Internet chatter as a means of monitoring potentially abusable opioid analgesics
Califano JA et al.	2004	"You've Got Drugs!" Prescription Drug Pushers on the Internet	USA	Analysis of the various methods and means by which prescription drugs are diverted for misuse, including fraudulent prescriptions, doctor shopping, pharmacy theft, patient distribution, Internet sales and international sales
Cicero TJ et al.	2008	Source of Drugs for Prescription Opioid Analgesic Abusers: A Role for the Internet?	USA	Description of Internet like a dangerous new avenue for the diversion of scheduled prescription opioid analgesics
Compton WM et al.	2006	Major increases in opioid analgesic abuse in the United States: Concerns and strategies	USA	Evaluation of abuse of opiate analgesics among teenagers in the United States: an investigation of best practices for treating pain in adolescents as well as the development of prevention strategies to reduce diversion and abuse
Drug strategies	2007	The Internet and Adolescent Non Medical Use of Prescription Drugs	USA	Analysis of Increasing adolescent non-medical use of highly addictive prescription opioid drugs
Forman, RF	2003	Availability of Opioids on the Internet	USA	Analysis of opiate-containing medications available online without a prescription
Forman RF et al.	2006	The Internet as a Source of Abuse	USA	The prevalence of NPWs in the Web and the availability of prescription opioid medications
Forman RF et al.	2006	The Availability of Web Sites Offering to Sell Opioid Medications Without Prescriptions	USA	The availability of Websites offering to sell opioid medications without prescriptions
Forman RF et al.	2006	Narcotics on the Net: The Availability of Web Sites Selling Controlled Substances	USA	State of art on NPWs
Frauger E et al.	2011	Which psychosocial prescription drugs are illegally obtained and through which ways of acquisition? About OPPIDUM survey	EU	Analysis of the different ways of drug acquisition, specially the illegal ways of acquisition
U.S. GAO	2003	Prescription drugs	USA	State of art on OxyContin
U.S. GAO	2004	OxyContin Abuse and Diversion and Efforts to Address the Problem.	USA	A simulation of purchase of narcotic pain medication without prescriptions on the Web
U.S. GAO	2004	Internet pharmacies	USA	A simulation of purchase of narcotic pain medication without prescriptions on the Web
Hydrocodone, an Addictive Narcotic Pain Medication, Is Available Without a Prescription Through the Internet	2001		USA	Investigation of the extent of information about hallucinogens available to Internet users
Halpern JH et al.	2001	Hallucinogens on the Internet: A Vast New Source of Underground Drug Information	USA	The prevalence of Internet use for the purchase of medications without a legitimate prescription, and the characteristics of those users
Inciardi JA et al.	2010	Prescription drugs purchased through the internet: Who are the end users?	USA	The study differentiates rates of nonmedical use of specific prescription opioids and provides other insights into individuals who nonmedically use opioids
Katz N et al.	2008	Internet-based Survey of Nonmedical Prescription Opioid Use in the United States	USA	Analysis of the clinical and legal implications and the ethics regarding the availability of prescription psychotropics over the Internet
Klein CA	2011	Psychotropics Without Borders: Ethics and Legal Implications of Internet-Based Access to Psychiatric Medications	USA	The potential impact of Internet based narcotics trade on addiction morbidities
Klein CA et al.	2011	www.nydrugdealer.com: Ethics and Legal Implications of Internet-Based Access to Substances of Abuse	USA	Effects of Opioid Dependence
Lieberman DZ	2001	Internet Facilitation of Opioid Dependence	USA	Analysis of five death Dextromethorphan-related
Logan BK et al.	2009	Five Deaths Resulting from Abuse of Dextromethorphan Sold Over the Internet	USA	Analysis of two cases of recreational use of Dextromethorphan by teenage boys
Murray S et al.	1993	Abuse of Over-the-Counter Dextromethorphan by Teenagers	USA	The availability in the UK population of prescription-only analgesics from the Internet
Raine C et al.	2008	The availability of prescription-only analgesics purchased from the internet in the UK	UK	Analysis on the effects of the abrupt discontinuation of Fioricet from the Web
Romero CE et al.	2004	Barbiturate Withdrawal Following Internet Purchase of Fioricet	USA	The comparison between doctor-patient relationship and the online pharmacies.
Weiss AM	2006	Buying prescription drugs on the Internet: Promises and pitfalls	USA	An assessment of the online availability of dextropropoxyphene for purchase over a time-span of 2 years
Schifano F	2006	On line availability of dextropropoxyphene over time, 2003-2005	UK	

Table 2. Controlled Substances Act (1970).

Controlled Substances Act (1970)				
Schedule I	Schedule II	Schedule III	Schedule IV	Schedule V
<p>The drugs included have a high potential for abuse and have no currently accepted medical use in treatment in the USA. There is a lack of accepted safety for use of the drug or other substance under medical supervision.</p> <p><i>Examples</i></p> <ul style="list-style-type: none"> - Heroin - Lysergic Acid Diethylamide - Marijuana - Methaqualone 	<p>The drugs included have a high potential for abuse and have a currently accepted medical use in treatment in the United States or a currently accepted medical use with severe restrictions. Abuse of the drug or other substance may lead to severe psychological or physical dependence.</p> <p><i>Examples</i></p> <ul style="list-style-type: none"> - Morphine - Phencyclidine - Cocaine - Methadone - Methamphetamine 	<p>The drugs included have less potential for abuse than the drugs or other substances in Schedules I and II. Furthermore, these drugs have a currently accepted medical use in treatment in the United States. Abuse of the drug or other substance may lead to moderate or low physical dependence or high psychological dependence</p> <p><i>Examples</i></p> <ul style="list-style-type: none"> - Anabolic steroids - Codeine - Hydrocodone - Barbiturates (some) 	<p>The drugs included have a low potential for abuse relative to the drugs or other substances in Schedule III. These drugs have a currently accepted medical use in treatment in the United States. Abuse of the drug or other substance may lead to limited physical dependence or psychological dependence relative to the drugs or other substances in Schedule III.</p> <p><i>Examples</i></p> <ul style="list-style-type: none"> - Dextropropoxyphene - Pentazocine - Meprobamate - Diazepam - Alprazolam 	<p>The drugs included have a low potential for abuse relative to drugs in Schedule IV. These drugs have a currently accepted medical use in treatment in the USA. Abuse of the drug or other substances may lead to limited physical dependence or psychological dependence relative to the drugs or other substances in Schedule IV.</p> <p><i>Examples</i></p> <p>Cough medicines with codeine are examples of Schedule V drugs</p>

References

- Allen, N. (2012). Batman Colorado shooting: James Holmes fixated by altered states of mind. The Telegraph. Available from: <http://www.telegraph.co.uk/news/worldnews/northamerica/usa/9419299/Batman-Colorado-shooting-James-Holmes-fixated-by-altered-states-of-mind.html> [last accessed 9 Jan 2014].
- Bailey, K., Richards-Waugh, L., Clay, D., Gebhardt, M., Mahmoud, H., & Kraner, J. C. (2010). Fatality involving the ingestion of phenazepam and poppy seed tea. *Journal of Analytical Toxicology*, 34, 527–532.
- Bert, F., Gualano, M. R., Brusaferrero, S., De Vito, E., de Waure, C., La Torre, G., Manzoli, L., Messina, G., Todros, T., Torregrossa, M. V., & Siliquini, R. (2013). Pregnancy e-health: A multicenter Italian cross-sectional study on internet use and decision-making among pregnant women. *Journal of Epidemiology & Community Health*, 67, 1013–1018.
- Boyer, E. W., & Wines Jr., J. D. (2008). Impact of Internet pharmacy regulation on opioid analgesic availability. *Journal of Studies on Alcohol and Drugs*, 69, 703–708.
- Butler, S. F., Venuti, S. W., Benoit, C., Beaulaurier, R. L., Houle, B., & Katz, N. (2007). Internet surveillance: Content analysis and monitoring of product-specific internet prescription opioid abuse-related postings. *The Clinical Journal of Pain*, 23, 619–628.
- Center for Disease Control and Prevention (CDC) (2011, November). Prescription Painkiller Overdoses in the US. CDC VitalSigns. Available from: <http://www.cdc.gov/vitalsigns/PainkillerOverdoses/index.html> [last accessed 9 Jan 2014].
- Compton, W. M., & Volkow, N. D. (2006a). Abuse of prescription drugs and the risk of addiction. *Drug and Alcohol Dependence*, 83, S4–S7.
- Compton, W. M., & Volkow, N. D. (2006b). Major increases in opioid analgesic abuse in the United States: Concerns and strategies. *Drug and Alcohol Dependence*, 81, 103–107.
- Controlled Substances Act (1970). Title 21 – Food and Drugs. Chapter 13 – Drug Abuse Prevention and Control. Subchapter I – Control and Enforcement. Washington, DC: US Department of Justice, Drug Enforcement Administration.
- de Waure, C., Cadeddu, C., Gualano, M. R., & Ricciardi, W. (2012). Telemedicine for the reduction of myocardial infarction mortality: A systematic review and a meta-analysis of published studies. *Telemedicine and e-Health*, 18, 323–328.
- Drug Enforcement Administration (DEA) (2001). Dispensing and purchasing controlled substances over the Internet. *Federal Register*, 66, 21181–21184.
- Drug Enforcement Administration (DEA) (2005). DEA Disables Major Pharmaceutical Internet Scheme: New “Virtual Enforcement Initiative” Announced, News Release, September 21, 2005. Washington, DC: Drug Enforcement Administration. Available from: www.usdoj.gov/dea/pubs/pressrel/pr092105.html [last accessed 9 Jan 2014].

Drugs.com – Drugs Information Online. Acetaminophen/hydrocodone side effects. Available from: <http://www.drugs.com/sfx/acetaminophen-hydrocodone-side-effects.html> [last accessed 9 Jan 2014].

Forman, R. F. (2003). Availability of opioids on the Internet. *Journal of the American Medical Association*, 290, 889.

Forman, R. F., & Block, L. G. (2006). The marketing of opioid medications without prescription over the Internet. *Journal of Public Policy & Marketing*, 25, 133–146.

Forman, R. F., Marlowe, D. B., & McLellan, A. T. (2006a). The Internet as a source of drugs of abuse. *Current Psychiatry Reports*, 8, 377–382.

Forman, R. F., Woody, G. E., McLellan, T., & Lynch, K. G. (2006b). The availability of Web sites offering to sell opioid medications without prescriptions. *American Journal of Psychiatry*, 163, 1233–1238.

Frauger, E., Nordmann, S., Orleans, V., Pradel, V., Pauly, V., Thirion, X., Micallef, J., & reseau des CEIPs. (2012). Which psychoactive prescription drugs are illegally obtained and through which ways of acquisition? About OPPIDUM survey. *Fundamental & Clinical Pharmacology*, 26, 549–556.

Gaul, G. M. (2003). Net Doctor Racks Up Business. *The Miami Herald* (December 28, 2003), 9A.

Gaul, G. M., & Flaherty, M. P. (2003). Internet Trafficking in Narcotics Has Surged. *The Washington Post* (October 20, 2003), A1.

General Accounting Office. (2004a). Testimony before the permanent subcommittee on investigations, Committee on Governmental Affairs, U.S. Senate, Statement of Marcia Crosse, Director, Health Care—Public Health and Military Care issues, June 17, 2004. Internet pharmacies: Some pose safety risks for consumers and are unreliable in their business practices (GAO-04-888T). Washington, DC: General Accounting Office. Available from: www.gao.gov/new.items/d04888t.pdf [last accessed 9 Jan 2014].

General Accounting Office. (2004b). Testimony before the permanent subcommittee on investigations, committee on governmental affairs, U.S. Senate, Statement of Robert J. Cramer, June 17, 2004. Internet pharmacies: Hydrocone, an addictive narcotic pain medication, is available without a prescription through the Internet (GAO-04-892T). Washington, DC: General Accounting Office. Available from: www.gao.gov/new.items/d04892t.pdf [last accessed 9 Jan 2014].

Gerstein, D. R., & Green, L. W. (1993). *Preventing Drug Abuse: What Do We Know?* Washington, DC: National Academy Press.

Giacometti, M., Gualano, M. R., Bert, F., & Siliquini, R. (2013). Public health accessible to all: Use of smartphones in the context of healthcare in Italy. *Igiene e Sanità Pubblica*, 69, 249–259.

Halpern, J. H., & Pope Jr., H. G. (2001). Hallucinogens on the Internet: A vast new source of underground drug information. *American Journal of Psychiatry*, 158, 481–483.

Inciardi, J. A., Surratt, H. L., Cicero, T. J., Kurtz, S. P., Martin, S. S., & Parrino, M. W. (2009). The “black box” of prescription drug diversion. *Journal of Addictive Diseases*, 28, 332–347.

International Drug Mart: With Record Number of Uninsured, Americans Turn to Foreign Pharmacies for Lowest-Cost Prescription Drugs. Yahoo News, June 11, 2008. Available from: <http://www.internationaldrugmart.com/media/yahoo-news-story.html> [last accessed 9 Jan 2014].

Internet World Stats (2012). Internet usage statistics, population and telecom reports for the Americas. Available from: <http://www.internetworldstats.com/stats2.htm> [last accessed 9 Jan 2014].

Johnston, L. D., O'Malley, P. M., Bachman, J. G., & Schulenberg, J. E. (2004). Monitoring the Future National Survey Results on Drug Use, 1975–2003. Vol. I: Secondary School Students. Bethesda, MD: National Institute on Drug Abuse.

Katz, N., Fernandez, K., Chang, A., Benoit C., & Butler, S. F. (2008). Internet-based survey of nonmedical prescription opioid use in the United States. *The Clinical Journal of Pain*, 24, 528–535.

Klein, C. A. (2011). Psychotropics without borders: Ethics and legal implications of internet-based access to psychiatric medications. *Journal of the American Academy of Psychiatry and the Law*, 39, 104–111.

Kronstrand, R., Roman, M., Thelander, G., & Eriksson, A. (2011). Unintentional fatal intoxications with mitragynine and O-desmethyl-tramadol from the herbal blend Krypton. *Journal of Analytical Toxicology*, 35, 242–247.

Kummervold, P. E., Chronaki, C. E., Lausen, B., Prokosch, H. U., Rasmussen, J., Santana, S., Staniszewski, A., & Wangberg, S. C. (2008). eHealth trends in Europe 2005–2007: A population-based survey. *Journal of Medical Internet Research*, 10, e42.

Lenhart, A., Madden, M., & Hitlin, P. (2005). *Teens and Technology: Youth are Leading the Transition to a Fully Wired and Mobile Nation* (p. 2). Washington, DC: Pew Internet and American Life Project.

Lieberman, D. Z. (2001). Internet facilitation of opioid dependence. *The American Journal on Addictions*, 10, 279–281.

Logan, B. K., Goldfogel, G., Hamilton, R., Kuhlman, J. (2009). Five deaths resulting from abuse of dextromethorphan sold over the internet. *Journal of Analytical Toxicology*, 33, 99–103.

Lu, S. (2003, September 29). Online Drug Sales: Promise or Peril? Yonkers, NY: Consumer reports webwatch. Available from: <http://consumersunion.org/news/online-drug-sales-promise-or-peril/> [last accessed 9 Jan 2014].

McCabe, S. E., Cranford, J., Boyd, C. J., & Teter, C. J. (2007). Motives, diversion and routes of administration associated with nonmedical use of prescription opioids. *Addictive Behaviors*, 32, 562–575.

National Association of Boards of Pharmacy. Verified Internet Pharmacy Practice Sites (VIPPS). Available from: [http://vipps.nabp.net/National Institute on Drug Abuse](http://vipps.nabp.net/National%20Institute%20on%20Drug%20Abuse). (2003). National Survey on Drug Use and Health (NSDUH). Bethesda, MD: NIDA.

Nielsen, S. B. (2009). Prescription drug misuse: Is technology friend or foe? *Drug Alcohol Review*, 28, 81–86.

Office of National Drug Control Policy (2004). Reducing Prescription Drug Abuse. Available from: http://www.whitehousedrugpolicy.gov/news/press04/prescrip_fs.pdf [last accessed 12 Oct 2012].

Official Journal of the European Union. (2011). DIRECTIVE 2011/62/EU OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 8 June 2011 amending Directive 2001/83/EC on the Community code relating to medicinal products for human use, as regards the prevention of the entry into the legal supply chain of falsified medicinal products. Available from: http://ec.europa.eu/health/files/eudralex/vol-1/dir_2011_62/dir_2011_62_en.pdf [last accessed 9 Jan 2014].

Ornes, L. H. (2006). Prescription drug re-importation: A balanced look. *Journal of Gerontological Nursing*, 32, 15–19.

Raine, C., Webb, D. J., & Maxwell, S. R. (2009). The availability of prescription-only analgesics purchased from the internet in the UK. *British Journal of Clinical Pharmacology*, 67, 250–254.

Rice, R. E. (2006). Influences, usage, and outcomes of Internet health information searching: Multivariate results from the Pew surveys. *International Journal of Medical Informatics*, 75, 8–28.

Schifano, F., Deluca, P., Baldacchino, A., Peltoniemi, T., Scherbaum, N., Torrens, M., Farre, M., Flores, I., Rossi, M., Eastwood, D., Guionnet, C., Rawaf, S., Agosti, L., Di Furia, L., Brigada, R., Majava, A., Siemann, H., Leoni, M., Tomasin, A., Rovetto, F., & Ghodse, A. H. (2006). Drugs on the Web; the Psychonaut 2002 EU project. *Progress in Neuro-psychopharmacology & Biological Psychiatry*, 30, 640–646.

Siemann, H., Schnell, J., & Scherbaum, N. (2009). Misuse and abuse of opioid analgesics – The role of the internet. Available from: <http://www.psychonautproject.eu/documents/presentations/SiemannHSchnellJScherbaumNPsychonautConference2009.pdf> [last accessed 9 Jan 2014].

Silicini, R., Ceruti, M., Lovato, E., Bert, F., Bruno, S., De Vito, E., Liguori, G., Manzoli, L., Messina, G., Minniti, D., & La Torre, G. (2011). Surfing the internet for health information: An Italian survey on use and population choices. *BMC Medical Informatics and Decision Making*, 11, 21.

Silicini, R., Saulle, R., Rabacchi, G., Bert, F., Massimi, A., Bulzomì, V., Boccia, A., & La Torre, G. (2012). Validation of a web-based questionnaire for pregnant women to assess utilization of Internet: Survey among an Italian sample. *Annali di Igiene: medicina preventiva e di comunità*, 24, 397–405.

Substance Abuse and Mental Health Services Administration. (2003). Overview of Findings from the 2002 National Survey on Drug Use and Health. Rockville, MD: Substance Abuse and Mental Health Services Administration, Office of Applied Studies.

Substance Abuse and Mental Health Services Administration. (2004). Mortality Data from the Drug Abuse Warning Network, 2002.

Rockville, MD: Substance Abuse and Mental Health Services Administration, Office of Applied Statistics. The Internet and Adolescent Non-medical Use of Prescription Drugs. Available from: <http://www.law.harvard.edu/programs/criminal-justice/kinsnida.pdf> [last accessed 9 Jan 2014].

The National Center on Addiction and Substance Abuse at Columbia University (2004 February). “‘You’ve Got Drugs!’” Prescription Drug Pushers on the Internet. A CASA white paper. United Nations (2007, January). International Narcotics Control Board Report 2006. Available from: http://www.incb.org/documents/Publications/AnnualReports/AR2006/AR_06_English.pdf [last accessed 9 Jan 2014].

Volkow, N. National Institute on Drug Abuse Research Report Series. Prescription Drug Abuse and Addiction. Available from: <http://www.drugabuse.gov/publications/research-reports/prescription-drugs> [last accessed 9 Jan 2014].

Weiss, A. (2006). Buying prescription drugs on the Internet: promises and pitfalls. *Cleveland Clinic Journal of Medicine*, 73, 282–288.